

**WHAT IS CLAIMED IS:**

1. A human coagulation Factor VII variant comprising a substitution of the Leu in position 305 of SEQ ID NO 1 with an amino acid residue selected from the group consisting of Val, Ile, Met, Phe, Trp, Pro, Gly, Ser, Thr, Cys, Tyr, Asn, Glu, Lys, Arg, His, Asp and Gln.
2. A Factor VII variant as defined in claim 1, wherein the substituted amino acid is selected from the group consisting of Val, Tyr, and Ile.
3. A Factor VII variant as defined in claim 1, further comprising a second substitution selected from the group consisting of (i) position 274; (ii) any of positions 300-304; (iii) any of positions 306-312; and (iv) combinations of any of the foregoing.
4. A Factor VII variant as defined in claim 3, wherein the second substitution is at position 274.
5. A Factor VII variant as defined in claim 3, wherein the second substitution is at any of positions 300-304.
6. A Factor VII variant as defined in claim 3, wherein the second substitution is at any of positions 306-312.
7. A Factor VII variant as described in claim 1, wherein the Leu residue in position 305 is the only amino acid residue that has been replaced relative to the sequence of SEQ ID NO:1.
8. A human coagulation Factor VII variant, comprising a substitution of the Leu in position 305 of SEQ ID NO 1 with Val.
9. A human coagulation Factor VII variant, comprising a first substitution of the Leu in position 305 of SEQ ID NO 1 with Val and a second substitution selected from the group consisting of: (i) substitution of Ala 274 with Met, Leu, Lys, or Arg; (ii) substitution of Arg 304 with Tyr, Phe, Leu, or Met; (iii) substitution of Met 306 with Asp or Asn; (iv) substitution of Asp 309 with Ser or Thr, and (iv) combinations of any of the foregoing.

10. A Factor VII variant as defined in claim 1, wherein the ratio between the activity of the variant and the activity of native Factor VII polypeptide having a sequence shown in SEQ ID NO 1 is at least about 1.25 when tested in an *in vitro* hydrolysis assay.
- 5
11. A Factor VII variant as defined in claim 10, wherein the ratio is at least about 2.0,
12. A Factor VII variant as defined in claim 10, wherein the ratio is at least about 4.0.
- 10 13. A human coagulation Factor VII variant comprising a substitution of the Leu in position 305 of SEQ ID NO 1 with an amino acid residue selected from the group consisting of Val, Tyr, and Ile, wherein the ratio between the activity of the variant and the activity of native Factor VII polypeptide having a sequence shown in SEQ ID NO 1 is at least about 1.25 when tested in an *in vitro* hydrolysis assay.
- 15
14. A nucleic acid construct comprising a nucleotide sequence encoding a Factor VII variant as defined in claim 1.
15. A recombinant vector comprising a nucleic acid construct as defined in claim 14.
- 20
16. A recombinant host cell comprising a nucleic acid construct as defined in claim 14.
17. A recombinant host cell as defined in claim 16, wherein the cell is of mammalian origin.
- 25 18. A recombinant host cell as defined in claim 17, wherein the cell is selected from the group consisting of CHO cells and BHK cells.
19. A transgenic animal comprising the nucleic acid construct defined in claim 14.
- 30 20. A transgenic plant comprising the nucleic acid construct defined in claim 14.
21. A method for producing a human coagulation Factor VII variant, which comprises (i) cultivating a cell as defined in claim 16 in an appropriate growth medium under conditions

09848107 050301

allowing expression of the nucleic acid construct and (ii) recovering the resulting polypeptide from the culture medium.

22. A method for producing a human coagulation Factor VII variant, which comprises  
5 recovering the variant from milk produced by a transgenic animal as defined in claim 19.

23. A method for producing a human coagulation Factor VII variant, comprising (i) cultivating a cell of a transgenic plant as defined in claim 20 under conditions in which the variant is expressed, and (ii) recovering the variant from the resulting plant.

10

24. A pharmaceutical composition comprising (i) a human coagulation Factor VII variant as defined in claim 1 and (ii) a pharmaceutically acceptable carrier or excipient.

25. A pharmaceutical composition comprising (i) a human coagulation Factor VII variant as  
15 defined in claim 2 and (ii) a pharmaceutically acceptable carrier or excipient.

26. A pharmaceutical composition comprising (i) a human coagulation Factor VII variant as defined in claim 3 and (ii) a pharmaceutically acceptable carrier or excipient.

20 27. A pharmaceutical composition comprising (i) a human coagulation Factor VII variant as defined in claim 7 and (ii) a pharmaceutically acceptable carrier or excipient.

28. A pharmaceutical composition comprising (i) a human coagulation Factor VII variant as defined in claim 8 and (ii) a pharmaceutically acceptable carrier or excipient.

25

29. A method for the treatment of bleeding episodes in a subject or for the enhancement of the normal haemostatic system, the method comprising administering to a subject in need of such treatment a therapeutically or prophylactically effective amount of a human coagulation Factor VII variant as defined in claim 1.

30

090403107 050301